Too Hot Isn't Healthy - Foods with very high capsaicin concentrations can damage health

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Capsaicinoids are responsible for the sharp, burning taste of certain fruits used as spices or vegetables, such as capsicum or chilli peppers. Capsaicinoids are e.g. capsaicin, dihydrocapsaicin and nordihydrocapsaicin. Capsaicin usually accounts for two-thirds to three-quarters of the total capsaicinoid content. Because extremely hot spicy sauces with high to very high capsaicinoid concentrations, are on the market in Germany too, the Federal Institute for Risk Assessment (BfR) has assessed the health risk posed by foods of this kind.

The BfR came to the conclusion that the oral intake of chilli fruits and preparations thereof on their own or as ingredients of hot to very hot dishes, such as those traditionally consumed in African, Arab, South American and Asian cuisine within the scope of the internationally accepted consumption, does not lead to any acute health effects. However, intolerances due to allergies are known. The BfR is assuming that the degree of hotness traditionally accepted by adults in the course of one meal equates to a maximum of one 5 mg dose of capsaicin per kg of body weight. This would correspond to an intake of 300 mg of capsaicin in one meal by an adult weighing 60 kg.

Serious health impairments have been observed with an excessively high consumption of chillies or chilli preparations. For the described undesired effects, such as irritation of mucous membranes, nausea, vomiting and hypertension, however, the dosage of capsaicinoids ingested by affected persons is unknown. In particular, children may react sensitively to hot chilli products. Severe cases of poisonings in small children after ingestion of chilli preparations are described in international literature.

On the basis of the available data, the BfR recommends that chilli and other spicy sauces with concentrations of more than 100 mg of capsaicin per kilogram of food (0.1%) should be labelled accordingly and that childproof closures should be applied to packaging. The BfR also recommends that the responsible food controlling authorities should check products with a capsaicin concentration of more than 6000 mg per kilogram on a case-by-case basis to establish whether they can be regarded as safe foods.

The BfR advises consumers to exercise caution with the intake of unusually large quantities of extremely hot chilli sauces and extracts, such as those encountered in "Fiery Foods Competitions". In these cases, severe health impairments may occur, such as hypertensive crisis which can be life-threatening under certain circumstances. In private households, hot chilli sauces should be stored out of the reach of small children.

1. Object and Background of the Assessment

The working group of food chemistry experts of the Länder and the Federal Office of Consumer Protection and Food Safety (ALS) has been concerned with the question how foods with high total capsaicin concentrations are to be assessed with regard to their marketability. The ALS made reference here to extremely spicy sauces and extracts available in the market. The background of the assessment inquiry is the current popularity of "Fiery Foods Competitions".

The BfR was requested by the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) to give its views on the facts outlined above from the point of view of risk assessment. The question as to which maximum “total capsaicin concentration" appears tolerable in extremely spicy foods sold directly to ultimate consumers, and if and when a warning notice as defined by Art. 14 Para. 3 b of Reg. 178/2002 has to be applied to foods, is of particular interest. As became evident from inquiries with the Hamburg Institute for Hygiene and the Environment, who submitted the question to ALS, “total capsaicin concentration” is understood to be the total concentration of capsaicinoids calculated as capsaicin in accordance with a method contained in the European Pharmacopeia, 6th Edition (2008) for quantified and refined cayenne pepper oil resin (Capsici oleoresina raffinata et quantificata) which includes the concentrations of capsaicin, dihydrocapsaicin and nordihydrocapsaicin.

The hotness of capsicum/chilli pepper-based products can be determined in so-called Scoville units (Scoville Heat Units, SHU). This was originally a purely sensory method in which the hotness of each concentration was “tasted” prior to further dilution. The hotness of the products can be determined analytically via the total capsaicin concentration. Total capsaicin concentration and Scoville can be mutually converted with a factor of 1 mg capsaicin/kg = 16.1 Scoville = 16.1 SHU (Thomas et al. 1998).

With regard to the risk assessment to be conducted, the BfR requested information from the Federal Office of Consumer Protection and Food Safety (BVL) as to whether any reports concerning poisoning or undesired effects after oral or other exposure (e.g. through skin or eye contact) to foods containing capsaicin (e.g. on the basis of peppers, *Capsicum* spp. fruits, chillies or cayenne pepper) were known to the BVL and if so what they were. Of greatest interest was information on the ingested doses of capsaicin and the other capsaicinoids mentioned above and their concentrations in the foods in question. With regard to the observation of exposure, the BfR also asked the BVL to provide data on the concentrations of capsaicin and, if available, the other capsaicinoids mentioned, as well as their sensory assessment.

The BfR also put the topic up for discussion at the 6th meeting of the BfR Commission “Assessment of Toxicopathic Diseases” on 11 May 2011.

The BVL notified that it had no reports of any undesired effects through exposure to foods containing capsaicin and that an inquiry had been lodged with the top regional authorities responsible for food monitoring in order to obtain the requested exposure data. The corresponding information on exposure observation was conveyed by the BVL on 18 July 2011.

In addition to this, the BfR was notified on 29 Mar. 2011 by the rapid alarm system about the draft of an RASFF report on a product examined by the Chemical and Veterinary Examination Office (CVUA) in Karlsruhe (information provided by the manufacturer on the label: 2,500,000 Scoville, which equates to 150,000 mg capsaicinoids/kg). Due to its extremely high concentration of capsaicinoids and the lack of dosage information and protective devices to prevent consumption by children, the product was regarded as capable of damaging health.

The BfR also received data from the CVUA Karlsruhe whereby capsaicin concentrations from 12,500 to 700,000 mg/kg (equivalent of 200,000 to 11,000,000 Scoville) had to be assumed in 10 chilli sauces and/or extracts.

In compliance with the question posed, the main focus of the assessment conducted by the BfR is on possible risks caused by acute exposure to capsaicinoids. Other chronic health

risks possibly caused by a high and regular intake of capsaicin over a longer period (questions of carcinogenicity) are not the subject of this assessment.

2. Result

Apart from intolerance caused by allergies, no serious health-damaging effects have been described for adults through the oral acute intake of chilli fruits and their preparations within the scope of the internationally customary and traditional consumption of dishes flavoured with hot and very hot spices. Where acute exposure is concerned, it is assumed that a dose of 5 mg capsaicin per kg body weight (BW) can be regarded as the traditionally accepted maximum hotness of a meal consumed by adults. The database is sketchy in regard to higher capsaicin intakes. Serious undesired effects have been described with the excessively high consumption of very hot chillies and chilli preparations. There are also reports of the death of an adult during a fiery foods competition, but the cause of death is unclear.

Severe cases of poisoning of children through the intake of chilli preparations as a result of accidents or child abuse are also known.

The BfR recommends that a note should be included on the label and safety caps applied to chilli sauces with concentrations of > 100 mg total capsaicin/kg for the protection of children and sensitive persons and to avoid irritations of the skin, mucous membranes and eyes.

The BfR is also questioning whether chilli sauces and chilli extracts with concentrations of > 6000 mg total capsaicin/kg should be regarded in general as safe foods as defined by Art. 14 of Reg. 178/2002 and recommends verification on a case-by-case basis.

The BfR recommends that consumers exercise extreme caution in regard to the intake of unusually large amounts of extremely spicy chilli fruits and chilli sauces, as encountered at fiery foods contests, as this may have health-damaging effects, such as hypertensive crisis, and can be life-threatening.

The BfR also advises that suitable preventive measures should be taken to prevent the accidental intake of hot chilli sauces by small children, which could be fatal.

3. Reasons

3.1 Risk Assessment

3.1.1 Agent

Capsaicinoids (acid amides of the vanillylamides with short-chain branched fatty acids) are responsible for the sharply burning taste of the fruits of many varieties of the genus *Capsicum* cultivated for use as spices or vegetables (chilli, paprika, peppers of the family Solanaceae, nightshade plants). Botanically speaking, the fruits of plants of the genus *Capsicum* are berries and not pods. Capsaicinoids include capsaicin (vanillylamide of the 8-methyl-6 nonenoic acid*;* n-*(*4-hydroxy-3-methoxybenzyl-8-*methylnon*-trans-6-*enamide;* CAS No. 404-86-4), dihydrocapsaicin (CAS No. 19408-84-5), and nordihydrocapsaicin (CAS No. 28789-35-7), (European Pharmacopeia [EP] commentary, 2011). Capsaicinoids in pharmacopeia quality 0.3 - 1 % are contained in dried cayenne pepper fruits (synonyms: Capsici fructus acer, piquante peppers, chili, chilli, Tabasco, peppers) derived from the family plants *Capsicum frutescens* L. s.l. (sensu latiore = more broadly) or *Capsicum annum* L. *IndP 66* , whereby the capsaicinoids mentioned occur in roughly the following concentrations: 63 - 77 % capsaicin, 20 - 32 % dihydrocapsaicin, 1 - 8 % nordihydrocapsaicin. Other capsaicinoids are homodihydrocapsaicin I and II, caprylic acid vanillylamide and nonylic acid vanillylamide. In addition to this, cayenne pepper fruits contain fatty oil, carotinoids, flavonoids, ascorbic acid and a complex mixture of volatile components. Capsaicin is soluble in ethanol, acetone and fatty oils and practically insoluble in cold water (EP comment, 2011; Hager, 2006).

Capsicum oleoresin (cayenne pepper oil resin) is understood to be a special extract of cayenne pepper fruits with comparatively high concentrations of capsaicinoids. The quantified and refined cayenne pepper oil resin (EP, 2008) contains 6.5 - 8.5 % capsaicinoids (EP comment, 2011; Peter, 2001).

Various varieties are derived from the genus *Capsicum*, the fruits of which differ in their degree of hotness. The species *C. annuum*, for example, not only includes the variety from which cayenne pepper fruits originate but also those varieties which produce the hot jalapeno and the mild bell peppers as fruits. Varieties of another species, *C. chinense,* produce sharp-tasting fruits of the types ”Habanero” and “Scotch Bonnet” (Peter, 2001; Roth, 2010). The variability of the concentrations of capsaicinoids in chilli fruits is not only due to the different botanical species and varieties but also to differences in the soil, light effects before and after harvesting, availability of water and various agricultural practices (Thomas et al.,1998; Bozokalfa et al., 2009; Pena-Alvarez et al. 2009).

Inside the chilli fruit, the placenta has the highest concentrations of capsaicinoids (Kozukue et al., 2005; Cisneros-Pineda et al., 2007; Bindu Thapa, 2009). Its removal prior to consumption would therefore result in a reduction of the concentrations.

Chilli sauces and extracts are manufactured using chilli fruits from many different botanical sources. Their degree of hotness is sometimes increased by adding Capsicum oleoresin (Zoschke, 2011).

To illustrate the point, the ALS compiled a table showing the total capsaicin concentrations and corresponding Scoville degrees (conversion: 1mg capsaicin/kg = 16 Scoville = 16 SHU) for several selected *Capsicum* fruits and/or preparations thereof (Table 1). Depending on

their provenance, paprika powders can also have higher total capsaicin concentrations than those listed in Table 1 (cf. Table 2).

Table 1

Example	Total Capsaicin	Scoville Degree (calculated)
Sweet bell pepper powder	<1 mg/kg	0 - 10
Paprika powder (piquant)	5 - 30 mg/kg	100 - 500
Tabasco sauce	100 - 300 mg/kg	1,600 - 5,000
Green jalapeno chillis, fresh	up to 500 mg/kg	2,500 - 8,000
Sambal oelek	up to 800 mg/kg	max 15,000
Chilli powder	1,000 - 3,000 mg/kg	30,000 - 50,000
Pure capsaicin (Sigma, >95 %)	>1 million mg/kg	16,000,000

The table in Enclosure 2 enables further comparison of the degrees of hotness of the fruits of various *Capsicum* varieties and various chilli sauces and extracts (Bützer, 2005).

In the food sector, the fruits of *Capsicum* varieties are used fresh, dried, smoked or pickled as whole fruits or ground into a powder (e.g. paprika or cayenne pepper as a spice) or flakes, consumed directly or used for the production of certain dishes, preparations, sauces or extracts (e.g. capsicum oleoresin, paprika oleoresin, paprika extract), whereby the aromatizing, heat-producing and/or colourizing properties of the fruits are used and the capsaicinoids concentrations of the preparations vary right down to a negligible level, such as in the food colourant Paprika Extract (E 160c) (Peter, 2001; Ternes et al., 2007).

3.1.1.1 Mechanisms of action

Through a reaction with the “transient receptor potential vanilloid subfamily 1” receptors (TRPV1), capsaicinoids lead to the stimulation of peripheral nociceptive neurones (e.g. C-fibres), i.e. the nerves responsible for the perception of damaging heat and pain stimuli. The stimulation provokes the release of the undecapeptide Substance P, CGRP (calcitonin gene-related peptide), somatostatin and vasoactive polypeptides. This initially produces a local neurogenic inflammation triggered by the mediators of Substance P (histamine, bradykinin, prostaglandins). This causes a sensation of heat on the skin and mucous membrane, painful burning and local hyperemia through vasodilation. The result of this with oral exposure is a sharp, burning perception which can still be felt with a dilution of 1:17,000,000. Depletion of Substance P causes phases of insensitivity which result in an analgesic effect and desensitization phenomenon. This also explains a reduction in sensitivity connected with regular intake. The onward transfer of the pain signal to the central nervous system, which is subdued after regular stimulation, could contribute to familiarization while the constant stimulation could lead to a partial degeneration of the neurones that contain TRPV1. Chronic intake of capsaicin results in damage to the affected neurones (Teuscher et al., 2004; Roth, 2010; Martindale, 2010; EP comment, 2011).

3.1.1.2 Applications other than in the food sector

Cayenne pepper fruits and their preparations are used in the pharmaceutical industry for the manufacture of preparations for external use (e.g. ointments, plasters) used to treat muscular and rheumatic pain. The concentrations of capsaicinoids are 0.005 to 0.01 %, in liquid preparations, 0.02 to 0.05 % in semi-solid preparations, and 10 to 40 µg/cm^2 in plasters (Commission E, 1990; EP comment, 2011). Ointments with which the concentrations of cayenne pepper preparations equate to 50 mg capsaicinoids (calculated as capsaicin) per 100 g of ointment are common (e.g. Fachinformation, 2008). Creams with up to 0.25 % capsaicin are available in some countries (Martindale, 2010).

In the cosmetic sector, *Capsicum* preparations and components are used as skin conditioners and odorants (Johnson, 2007).

Oleoresin capsicum (OC) is the main active ingredient (irritant) in the so-called pepper sprays which are sprayed over a distance of several metres and which are intended to neutralize people's ability to attack or defend themselves (Jesse, 2009). The concentration of Oleoresin capsicum in the spray is 5 - 15 %, whereby the capsaicinoid concentrations of the Oleoresin capsicum vary between 1.2 and 12.6 % (Smith and Stopford, 1999).

Capsaicin is also used in animal repellent sprays (Jesse, 2009) and as a pesticide in the USA (EPA, 1992; Federal Register, 2010; Albert and Schneller, 2009).

3.1.2 Legal provisions in the food sector

In accordance with Art. 6 Para. 1 in connection with Appendix III, Section A of Reg (EC) 1334/2008, capsaicin as such may not be added to foods. The regulation has been in force since 20 Jan. 2011. It must be assumed that the adding of Oleoresin capsicum to foods to increase their degree of hotness is not affected by this ban.

3.1.3 Risk potential

Main emphasis regarding the description of the risk potential is placed on observations of acute toxicity after oral ingestion by humans and animals.

3.1.3.1 Assessment by international committees

Capsaicin was evaluated by the Scientific Committee on Food (SCF) (SCF, 2002).

In the opinion of the SCF of 26 Feb. 2002 it is stated that capsaicin, capsaicinoid mixtures, chillies and chilli extracts were toxicologically tested after oral application in mice, rats and hamsters. Several of these studies suggest a cancerogenic potential. These studies are not fully conclusive, however, and a more recent study shows no cancerogenic effects in mice. High chilli consumption in humans has been described as a cancer risk factor for the gastrointestinal tract, probably as a result of the irritating effect that capsaicinoids have on the mucous membranes. The SCF also made specific mention of the induction of genotoxic effects through capsaicin *in vitro* and *in vivo*. In synopsis, the SCF comes to the following conclusions:

"The Committee concluded that the available data did not allow it to establish a safe exposure level for capsaicinoids in food."

The human intake of capsaicinoids in India, Thailand and Mexico, where capsicum spices are heavily consumed, has been estimated to be 25 - 200 mg/day. The high consumption of chillies in Mexico and India was reported to be associated with cancer of the upper digestive tract. In contrast, the maximum daily intake from mild chillies and paprika in Europe was roughly estimated to be 1.5 mg/day. In the one study conducted in Europe, no increase in the incidence of gastric cancer was found in association with occasional and lower intakes of chillies." (SCF 2002)

Capsaicin was also evaluated by the Committee of Experts on Flavouring Substances of the Council of Europe (2005). The committee concluded that the data on cancerogenicity in humans and animals were contradictory and in particular that no sufficient data on epidemiology are available. The following maximum values for the concentration of total capsaicinoids were proposed:

- Beverages and other foods: 5 mg/kg
- Spicy drinks and foods: 10 mg/kg

The following exceptions should be considered for spices and sauces:

- Hot ketchup and similar products: 20 mg/kg
- Tabasco sauce, harissa, hot pimento oils and similar products: 50 mg/kg.

3.1.3.2 Animal testing data on the acute toxicity of capsaicin and chilli sauce (focus on oral ingestion)

Glinsukon et al. (1980) administered capsaicin in a mixture of ethanol, Tween 80 and a saline solution through a gastric feeding tube to 30 male Swiss Albino mice and determined an LD_{50} of 60 - 75 mg/kg body weight (BW). 63 male mice of the same strain were treated in the same way with capsaicin in dimethylsulfoxide (DMSO), producing an LD_{50} of 190 mg/kg BW. A desquamative necrosis with increased formation of mucous of the stomach lining was determined per microscope in the bodies of the dead animals, but there were no histopathological changes in other organs. Working on the basis of a minimum intragastral capsaicin dose of roughly 100 mg, the authors estimate that this quantity would be contained in approximately 32.4 g of *Capsicum* fruits (dry weight), which would equate to an intake of 1.94 kg of dried capsicum fruits by a person weighing 60 kg. The LD_{50} for intratracheally administered capsaicin in DMSO determined in mice of the same strain was 1.60 mg/kg BW and therefore only a fraction of the oral LD_{50}.

Saito and Yamamoto (1996) administered capsaicin in propylene glycol in a one-off oral dosage (96, 116, 139, 167, 200 mg/kg BW) to CD rats and Crj:ICR mice, whereby each dosage group consisted of 10 female and 10 male animals per species. With the mice, an LD_{50} for capsaicin of 118.8 mg/kg BW was determined for the males and 97.4 mg/kg BW for the females. With the exception of the two low-dosage groups, more than 60 % of the mice in each group died. After treatment, the animals showed signs of salivation, tonic and clonic convulsions, dyspnoea, tremor, cyanosis, gait disorder, bradypnoea and erythema on the skin. With the rats, the LD_{50} for capsaicin was 161.2 mg/kg BW with the males and 148.1 mg/kg BW with the females. The toxic symptoms were similar to those of the mice, but the indications of cyanosis, tonic and clonic convulsions and dyspnoea were higher with the rats. The authors assume hypotonia and respiratory paralysis as the cause of death in both animal species. The histopathological examinations revealed slight focal erosions, ulcers and increased quantities of mucous in the stomachs of all dead animals. Several of the dead animals also showed evidence of haemorrhaging in the gastric fundus. The liver, gall bladder and kidneys

did not show any changes either macroscopically or microscopically among the dead and surviving animals.

Winek et al. (1982) examined the toxicity of Tabasco® Pepper Sauce on the basis of red *Capsicum* fruits (red peppers) and vinegar. 6 groups, each consisting of 7 male and 7 female Sprague Dawley rats were administered the sauce in volumes of 8, 12, 18, 27, 40.5 and 60.75 ml/kg BW per gastric feeding tube (orogastric intubation). The LD_{50} of the sauce for the male animals was 23.58 ml/kg BW and 19.52 ml/kg BW for the females. The authors calculated a theoretical LD_{50} value of 400 ml of sauce for a child weighing 20 kg and 1400 ml for an adult weighing 70 kg. Prior to death, the animals showed signs of hypothermia, tachypnoea and lethargy. The autopsy showed no evidence of ulcers, perforation or bleeding in the gastrointestinal tract. All organs appeared normal macroscopically.

Nopanitaya et al. (1974) administered either an aqueous extract of *Capsicum* fruits (10 g of ground fruits in 100 ml 0.9 % NaCl, 5 min 100º, strain off) or 0.014 % capsaicin in 0.9 % NaCl, each in volumes of 2 ml through intragastral tubes, to groups of 6 male Sprague Dawley rats and examined the effect on the mucous membrane of the duodenum with exposure times of 2, 6, 15, 30, 45 and 60 min. The damage to mucous membrane cells, as evidenced by the swelling of the mitochondria, increased number of free ribosomes and lysosomes and shrinkage of the cell cores, for example, increased with the time of exposure. The authors are assuming that the quantity of capsaicin administered (roughly 1 mg capsaicin/kg BW) is equivalent to the average quantity of capsaicin ingested by the rural population of Thailand in one meal.

3.1.3.3 Animal testing data on the acute skin and eye tolerance of chilli sauce

Winek et al. (1982) examined the acute dermal reaction with the non-occlusive application of Tabasco® Pepper Sauce to New Zealand albino rabbits with which 6 ml of the sauce was applied to an area of 10x15 cm^2 depilated damaged or undamaged skin (3 males and 3 females per group). 4 of the 6 animals with pre-damaged skin resisted the application for several seconds with accompanying vocalizations. These animals showed the most distinct reactions after 24 hours in the form of severe erythemas and edemas, dark red scabs and the formation of exudate. All of the other animals showed defined erythemas and slight edemas. 72 hours after the treatment, all of the animals showed forms of desquamation and sloughing (Winek et al., 1982).

After 0.1 ml of Tabasco®Pepper Sauce had been applied to the conjunctival sac of the left eye (the right eye served as a control) of New Zealand albino rabbits (3 groups of 3 males and 3 females), the eyes were rinsed after 7-10 seconds in the first group, after 2-5 seconds in the second group and not at all in the third. The eye damage was assessed after 1, 2, 3, 7, 14 and 21 days. 15 of the 18 animals reacted with vocalization and all of them resisted the treatment. Conjunctivitis, chemosis and exudation developed within 90 minutes. 24 hours after the treatment, moderate to severe conjunctival damage was detected in all of the test animals, but most distinctly in the ”no eye wash” group which also showed the greatest damage to the cornea and iris, which was not so severe in the other groups. While the damage to the conjunctival sacs and cornea diminished in the course of 72 hours after administration, the iris damage intensified with some animals. After 7 days, the conjunctival damage had diminished in all but 3 animals in the “no eye wash” group (Winek et al., 1982). The same experiment was carried out with 0.1 ml of 5 % white distilled vinegar, which is an ingredient of Tabasco® Pepper Sauce along with the capsaicin. The application did not cause any complaints in the animals. Compared to the findings observed after the application of the sauce, the vinegar treatment induced a comparable reddening, chemosis and lacrimation but

considerably less damage to the cornea and iris. The eyes of all animals treated with vinegar appeared normal 14 days after the treatment (Winek et al., 1982).

In a sensitization test in which 0.1 ml of Tabasco® Pepper Sauce was rubbed into depilated, slightly damaged skin areas of albino guinea pigs (application repeated 3 times a week, total of 9 applications, test repeated after a break of 2 weeks), no skin reaction or sensitization was determined with the test animals that differed from the control animals.

3.1.3.4 Human data on acute toxicity (mainly oral administration)

3.1.3.4.1 Studies

In a double-blind, randomized study, 8 healthy probands were asked to ingest either the spices cayenne pepper (0.1, 0.5 and 1.5 g; with BW = 60 kg equivalent to 1.7, 8.3 and 25 mg/kg BW) or black pepper (1.5 g) or 625 mg aspirin (positive control) suspended in 100 ml of water. The intake of water served as a negative control. The dose of 1.5 g of cayenne pepper was regarded as equivalent to the consumption of a very spicy meal. 30 min after consumption, a series of gastric lavages was conducted and the acquired liquid examined. After ingesting cayenne pepper and black pepper in doses of 1.5 g and aspirin, significant increases in the discharge of parietal cells, pepsin secretion and potassium excretion, as well as the exfoliation (desquamation) of stomach cells were determined. The occurrence of minor haemorrhaging of the mucous membrane after the administration of cayenne pepper was considered to have been connected with the different levels of sensitivity of the probands. The medium dosage of cayenne pepper can be regarded as NOAEL (No Observed Adverse Effect Level). The authors conclude that the effects of the long-term intake of the spices are uncertain (Myers et al., 1987).

Milke et al. (1995) administered 3 x 1 g (3 g/day) of cascabel chili with 880 mg capsaicin/kg or ancho chilli with 488 mg capsaicin/kg to 12 healthy probands in a randomized study on one day. The determination of the Johnson De sample index showed that viewed as a whole, chilli intake increases gastroesophageal reflux, whereby only the increase of the effect caused by cascabel chilli was significant in the individual evaluation.

Graham et al. (1988) concluded from a study in which probands were exposed to jalapeno fruits and piquant peppers in different ways, partly with meals, that the consumption of spicy foods by healthy people is not associated with endoscopically detectable gastroduodenal mucous membrane damage.

3.1.3.4.2 Case descriptions, reports on experience

Apart from the cases of allergically induced intolerance described below, the relevant literature only contains details of the known effects associated with capsaicin intake for the oral acute ingestion of chilli fruits and their preparations within the scope of the internationally customary and traditional consumption of dishes flavoured with hot and very hot spices: stimulation of salivation, the secretion of gastric juices, sweat and gastric motility, the perception of hotness and burning in the mouth and irritation of the stomach lining (EP comment, 2011; Hager, 2006; Peter, 2001). There are no reports of any more severe acute undesired or health-damaging effects within the scope of traditional consumption.

3.1.3.4.2.1 Excessive consumption, fiery foods contests

The BVL announced on 02 May 2011 that they had received no reports of the occurrence of undesired effects after the ingestion of foods containing capsaicin.

The inquiry made by the BfR at the 6th meeting of the BfR Commission "Assessment of Toxicopathic Diseases" on 11 May 2011 revealed that the poison information centres in Zürich and Freiburg did not have any knowledge of cases of undesired effects after the ingestion of hot chilli sauces with high concentrations of capsaicin. No instances of this kind have been reported to the BfR to date by the other information centres requested to do so.

In addition to this, however, while conducting research in the internet, the following case description was found in the German daily press which does not permit any scientific assessment regarding causality, additional influencing factors and the dose-effect relationship, because no information is available on the composition and quantities of the products consumed and the individual symptoms of poisoning. It was reported in the daily press on 20 Jan. 2010 that 10 secondary school children in Augsburg required emergency treatment as a result of a dare. The adolescents had ordered a particularly hot chilli sauce through the internet and were having a drinking contest at school. Ten of the eighth grade pupils subsequently complained of extreme nausea and were treated by the casualty doctor and eight of them were admitted to the paediatric hospital in Augsburg for further treatment and observation (Abendzeitung München, 2010; TZ-online, 2010; Shortnews, 2010; Rettungsdienst.de, 2010).

At the end of September 2008, there were reports in the British daily newspapers of a death after the consumption of hot chilli sauce during a competition, whereby the possibility of an anaphylactic shock was discussed (New Scientist, 2008; Times Online, 2008; The Telegraph, 2008). With the amount of information available, the causal relationships have to be regarded as unclear.

At a Texan fiery foods contest in which 3 female and 2 male participants had to eat as many jalapeno fruits as possible within the space of 3 minutes, 3-13 fruits were consumed (median: 5 fruits). 3 of the contestants ascertained epiphora and rhinorrhoea immediately after consumption and one man suffered from dysuria. 4 of the 5 participants observed a burning sensation during defacation within the 24-hour period after the contest (Diehl and Bauer, 1978).

After consuming excessive quantities of "peppers and chili peppers" (no further dosage information), 2 of the men were diagnosed the next day with arterial hypertensive crisis which in one case occurred accompanied by acute cardiac infarction associated with increased values of thyroid stimulating hormone (Patané et al., 2008; Patané et al., 2010).

3.1.3.4.2.2 Exposure of children

Further research also revealed incidences of poisoning with foods containing capsaicin among children as a result of accidents and child abuse.

Snyman et al. (2001) report on the death of an 8-month-old boy in South Africa who, after suffering from severe coughing for 7 days and diarrhoea and vomiting for 3 days, was admitted to hospital with shock, acidosis, central cramps, prerenal failure and septicaemia and died the same day after suffering two cardiac arrests. The boy had been given an oral infusion of a red powder containing “red pepper” (dosage and frequency unknown), which is used as a traditional medicine (name in Afrikaans: “rooipoeier”). Capsaicin was detected in the powder. The pathological examination established that the liver was discoloured and enlarged.

In spring 2011, a British newspaper reported the case of the emergency rescue of a 10-month-old boy who became unconscious after apparently accidentally ingesting chilli sauce and who suffered serious respiratory restrictions after his face turned a blue-red colour. The degree of hotness of the sauce is not known (Castle, 2011).

Tominack and Spiker (1987) report on the abuse of 3 children aged 3, 5 and 7 years who were forced to keep a split jalapeno fruit or Tabasco sauce in their mouths for 15-20 minutes. The children suffered from burning in the mouth, throat and stomach, as well as during defacation, and from vomiting and diarrhoea.

With the death cited in literature of a 33-month-old boy after apnoea as a result of abuse through the “ingestion of pepper”, it is not clear whether black pepper or red pepper was involved (Dine and McGovern, 1982).

3.1.3.4.2.3 Hypersensitivity reactions/intolerances

In rare instances, a hypersensitivity reaction to cayenne pepper can occur which can also be induced by oral exposure. Urticaria, generalized eczema and respiratory complaints have been described as symptoms. Sensitization frequently occurs here through vocational exposure, e.g. in the butcher’s trade or spice production. Asthmatics could be very susceptible to hypersensitive reactions to capsaicin (Gimenez and Zacharisen, 2011; Leitner et al., 1998; Schöll and Jensen-Jarolim; 2004; Rance and Dutau; 1997; Zuskin et al., 1994; Feldman and Levy; 2003; Dikensoy and Bayram, 2001; EP comment, 2011).

With repeated contact with chilli fruits, e.g. in the preparation of food, severe contact dermatitis can occur in the form of burning pains, erythema and hyperesthesia in the palms of the hands (“Hunan hand”) (e.g. Williams et al., 1995; Hager, 2006).

3.1.3.4.2.4 Medications for dermal application

The pharmacological effects connected with the topical application of pharmaceutical preparations containing capsaicin are known. It is described, for example, that after applying ointments containing cayenne pepper thick extract in a concentration containing 50 mg of capsaicinoids (calculated as capsaicin)/100g, it frequently ($\geq$1% to <10% of applications) results in a burning or piercing pain with accompanying reddening and heat development which has to be tolerated in the interest of the therapeutic effect (e.g. Fachinformation, 2008).

In the pharmaceutical sector, however, reference is also made to the fact that use of preparations of this kind with an existing hypersensitivity or allergy to cayenne pepper preparations is contraindicated. In addition to this, warning notices and precautionary measures provided for these preparations (e.g. Fachinformation, 2008):

"(i) Cayenne pepper preparations severely irritate the mucous membranes, even in small doses, and produce a painful burning sensation. (ii) For this reason, the ointment should not be allowed to make contact with the eyes, mucous membranes or open wounds. (iii) If the ointment does make contact with the eyes, an eye specialist should be consulted without delay. Thorough rinsing of the eye with copious amounts of cold water is recommended as an emergency measure. (iv) Do not apply to damaged skin, e.g. after burns and injuries or with inflammations and eczemas…... (v) The hands should be washed thoroughly after applying the ointment to avoid unintentional contact with other parts of the body. … (vi) Children: No sufficient tests have been conducted in regard to the use of this medication with children. It should therefore not be used by children aged under 12 years."

3.1.3.4.2.5 Undesired effects through the use of pepper spray

When pepper spray is used, capsaicin is ingested by inhalation. For this reason, in addition to undesired mucous membrane effects (epiphora, irritation of the eyes and mucous membranes in the nose) and skin irritations, the focus is on symptoms in the upper respiratory tract and bronchial system as a result of irritation through capsaicin (Olajos and Salem, 2001; EP comment, 2011). Inhalation also leads to bronchoconstriction, inflammation of lung tissue and damage of the respiratory cells (Fuller et al., 1985; NPIC, 2011). For this reason, the findings on the use of pepper spray can only be transferred to the question posed here to a very limited extent. The deaths that occurred after the use of pepper spray were investigated more thoroughly (Olajos and Salem, 2001; Smith et al., 2002; Steffee et al., 1995). Of the 32 deaths analyzed in a study, a causal connection was identified in only one case, an asthmatics (Smith et al., 2002; Steffee et al., 1995).

3.1.3.5 Exposure

3.1.3.5.1 Concentrations

Data on total capsaicin concentrations were requested from the federal states (Laender) by the Federal Office of Consumer Protection and Food Safety (BVL) and supplemented by literature research.

The BVL does not have any information on the sensory assessment of samples in connection with measured capsaicin concentrations. 13 samples (4 x spice preparations for meat in the meat processing sector, 2 x soya sauces, 3 x paprika powders, 3 x spice mixtures, 1 x spicy sauce/paste not specified more precisely) without information on capsaicin concentrations were tested for their taste but no abnormalities were detected. In addition to the transfer of individual data, the BVL pointed out to the BfR a sample which raised objection from the Chemical and Veterinary Examination Office in Karlsruhe. Even after dilution of 1:100 in oil, the sample was still described as "very hot, burning" with long-lasting irritation and therefore and for the lack of dosage instructions and a child-proof closure assessed as "capable of damaging health".

Details of capsaicin concentrations are available for 44 samples which were measured by the Control Authority of the Land of Saxony and the Chemical and Veterinary Examination Office in Karlsruhe. Dihydrocapsaicin was also detected in five of these samples. The data trans-

ferred to BVL contain one suspect sample which is excluded from the statistical evaluation in Table 2 and discussed separately. The country of origin is known in 30 cases, with 22 samples originating in Germany, 3 in Thailand, 2 in Tunisia and one in Switzerland, Vietnam and the USA, respectively. Due to the small number of samples, systematic differences in the concentration data by country of origin cannot be verified, but all values over 100 mg/kg come from Germany.

The suspect sample mentioned above not evaluated in Table 2 is a chilli sauce from Germany with a total capsaicin concentration of 52,885 mg/kg (30,088 mg/kg capsaicin and 22,797 mg/kg dihydrocapsaicin). No additional information was available which could help to clarify the type of sample and the reason for the high concentration.

Table 2: Capsaicin, dihydrocapsaicin, total capsaicin concentrations in foods based on the measurements of the food monitoring authorities from 2009-2011 [mg/kg]

	Qty.	Definable	Minimum		Median		Mean		Maximum	
			LB	UB	LB	UB	LB	UB	LB	UB
Capsaicin										
Spicy sauces/ pastes (chilli sauce, sambal)	23	43%	0	1	0	4	33	35	245	245
Chilli (powder or dried)	6	100%	79	79	289	289	325	325	813	813
Paprika powder	14	71%	0	2	18	18	41	42	207	207
Dihydrocapsaicin										
Spicy sauces/ pastes (chilli sauce, sambal)	2	100%	53	53	68	68	68	68	83	83
Chilli (powder or dried)	1	100%	65	65	65	65	65	65	65	65
Paprika powder	1	100%	123	123	123	123	123	123	123	123
Total capsaicin										
Spicy sauces/ pastes (chilli sauce, sambal)	23	43%	0	1	0	4	39	41	328	328
Chilli (powder or dried)	6	100%	79	79	289	289	336	336	813	813
Paprika powder	14	71%	0	2	18	18	50	51	330	330

The difference shown in Table 2 between the lower bound (LB) (all undefinable values set to 0) and the upper bound (UB) approach (all undefinable values set to the quantitation limit, non-detectable values to the detection limit) is to be regarded as slight, which is why reference is only made below to the upper bound values.

Compared to the data of the German food monitoring authorities evaluated in Table 2, according to the information on the packaging Tabasco sauce has a degree of hotness of 600 - 5,000 Scoville, which equates to 37 - 311 mg/kg capsaicin after conversion with the factor 16.1 (Thomas et al. 1998). Bibliographical references to the capsaicin concentrations in chilli fruits, sauce and spicy sauce are also compiled in Table 3. Comparison with Table 2 shows that the concentrations in the upper range of distribution may still be underestimated. It should be noted, however, that the bibliographical references relate mainly to the Asian and Central American regions where the use and variety of chilli fruits are more widely distributed than in Germany. One uncertainty in the comparison of data from various sources results from the varying relative percentages of individual capsaicinoids in the total capsaicin concentration (Choi et al. 2006). In the bibliographical references, dihydrocapscaicin was always quantified in addition to capsaicin, but the capsaicinoids analyzed further and calculated into the total are not uniform. Theoretically, the results for individual fruits would be required for acute exposure. As can be taken from Table 3, examinations of fresh chilli fruits also included pooled samples which could lead to an underestimation of the concentrations in fresh chilli fruits under certain circumstances.

Table 3: Overview of concentrations of total capsaicin from various literature sources [mg/kg]

	Min	Max	Source	Remarks
Chilli fruits, fresh	131		Choi et al. 2006	Korean market, 3 samples pooled
	622	765	Perucka et al. 2000	
	18.7	2,261	Kozukue et al. 2005	Fresh fruits, whole and canned
	<10	8,550	Lopez-Carrillo 2003	15-20 pooled chilli fruits in each sample
Chilli fruits, dried	110	1,440	Lopez-Carrillo 2003	15-20 pooled chilli fruits in each sample
Chilli spice	425	3,530	Choi et al. 2006	Korean market, 3 samples pooled
	890	1,410	Peusch et al. 1997	Chilli powder originating in the USA
Spice sauces	44.2	3,752	Choi et al. 2006	Foods commercially available in Korea, 3 pooled samples in each case
	48	84	Takahashi et al. 2008	mg/L
	5	852	Pena-Alvarez et al. 2009	
Foods	71	85	Choi et al. 2006	Chinese noodles, mild and hot, commercially available in Korea, 3 pooled samples in each case

Table 4: Scoville units and capsaicin concentrations for various spicy sauces conveyed by the CVUA Karlsruhe

Designation	Scoville	Capsaicin [approx. mg/kg]
Sample 1	200,000	12,500
Sample 2	500,000	30,000
Sample 3	650,000	40,000
Sample 4	800,000	50,000
Sample 5	1,000,000	65,000
Sample 6	1,000,000	65,000
Sample 7	1,200,000	75,000
Sample 8	1,500,000	100,000
Sample 9	1,500,000	100,000
Sample 10	11,000,000	700,000

The example given above and the seven control and three suspect samples listed in Table 4 reported by the CVUA Karlsruhe show, however, that hot sauces may have higher concentrations than that of the suspect sample reported by the BVL and are also produced and advertised specifically for the German market. For this reason, the sauces from the range of another company are compared additionally in Table 5. As the capsaicin concentration was not listed on the packaging here and no measuring results are available, the Scoville units listed on the package were converted into concentrations using a factor of 16.1 (Thomas et al. 1998). This means that the sauces reported by the CVUA Karlsruhe as well as those marketed by the company have concentrations that are considerably higher than those taken from food monitoring for Germany. According to the internet research conducted, all of the sauces listed in Table 4 contain specific notes on consumption.

Table 5: Scoville units and the capsaicin concentrations calculated from them for various spicy sauces available in Germany

	Scoville units according to the manufacturer's website[1]	Calculated capsaicin concentration [mg/kg]	Remarks
BBQ Sauce Sample 1	2,500-5.000	155-311	
BBQ Sauce Sample 2	10,000	621	
Chilli Sauce Sample 1	80,000-85,000	4,969-5,280	
Chilli Sauce Sample 2	80,000-85,000	4,969-5,280	
Chilli Sauce Sample 3	38,500-45,000	2,391-2,795	Advertised by the manufacturer as a "beginner" product
Chilli Sauce Sample 4	80,000-95,000	4,969-5,900	Warning notice on the package: "Keep out of the reach of children", "Avoid eye and skin contact"/ Use as directed on package, including "Undiluted with barbecues and grilled sausages and with all meat and poultry dishes"/ Listed in product specification under "Additive for the seasoning of foods". Suitable in diluted form for all groups of persons.
Chilli Sauce Sample 5	80,000-100,000	4,969-6,211	
BBQ Sauce Sample 3	4,000-5,000	248-311	
BBQ Sauce Sample 4	200,000	12,422	Notice on package "Do not consume undiluted", according to internet information, only available through the internet
Pepper Extract Sample 1	400,000	24,845	Notice on package: "Please observe the directions for use", according to internet information, not for sale to persons under 16 years of age, notice in the internet: "Use only a few drops at a time", pipette and child-proof closure
Pepper Extract Sample 2	1,200,000	74,534	Notice on package: "Please observe the directions for use", notice in the internet: "Use only a few drops at a time", according to photo, probably with pipette and child-proof closure

[1] Information provided by each manufacturer

With up to 2,795 mg/kg of capsaicin, the sauces advertised by a company as a "beginner package" are in the upper range of the values compiled in Table 3 from the bibliography. With up to 5,900 mg/kg, many sauces reach almost twice this value. The form in which these sauces are consumed cannot be determined unequivocally. The product specifications for the chilli sauces in samples 3 and 4 state: "Additive for the seasoning of foods. Suitable for all groups of persons when diluted". This could lead indirectly to the conclusion that the sauces are diluted or consumed in quantities comparable to Tabasco sauce. Contrary to this, the text on the package states: "Undiluted with barbecues and grilled sausages and with all meat and poultry dishes", as is also stated on the labels of the chilli sauces in samples 1 and 2, which are clearly to be used as barbecue sauces and ketchup. Accordingly, it is assumed here that sauces in these concentration ranges are consumed in quantities comparable to other barbecue sauces and ketchup.Concentrations in extracts not intended for undiluted consumption may exceed these in sauces and ketchups by far, but they are further not considered in the following paragraphs due to a lack of information on the type of dilution, dosage, pipetting where applicable, child-proof closures and restricted marketing.

3.1.3.5.2 Consumption

The evaluations are based on the data of the two independent 24h recalls of National Consumption Study II (NVS II), which was collected in a computer-supported interview by means of ”EPIC-SOFT” (MRI 2008, Krems et al. 2006). The data of 13,926 persons who had both interviews available to them were evaluated. Because consumption data for individual days are available, the 24h recall method is suitable for making exposure estimations with acute as well as chronic risks.

To estimate the acute risks the higher quantity of the two 24 h recall values for each person is taken. The 95th percentiles and maxima of the respective food intake are calculated for the consumers as a conservative estimate shown in Table 6. Accordingly, it can be observed that the maximum consumed quantity in one meal for chilli sauces, other barbecue sauces and ketchup are in the same scale with a 95th percentile of 100 g and 120 g. The same applies to dried chilli fruits, chilli and paprika spice, the 95th percentile of which is set at the same level as the maximum due to the small number of cases. The latter lies between 4 g per portion and 20 g per portion. Chilli fruits, fresh or preserved, have a 95th percentile of almost 50 g per portion. Systematic differences with regard to age and sex cannot be derived from the data (presumably due to the small number of cases) and are not presented for this reason.

Table 6: Maximum consumption quantity over 2 days in g per portion (basis: consumers only)

	N	P95	Max
All persons questioned	13,926		
Chilli sauces	67	120.0	200.0
Other barbecue sauces	184	120.0	200.0
Ketchup	1,251	100.0	360.0
Chilli fruits, friesh or preserved	141	47.0	100.0
Chilli fruits, dried	8	20.0	20.0
Chilli, spice	2	7.0	7.0
Paprika, spice	3	3.7	3.7
Tabasco sauce	6	2.5	2.5

3.1.3.5.3 Capsaicin intakes

To evaluate acute risks, a one-off high load has to be determined as a reference. For that purpose, various scenarios are derived from the concentration data. The highest value documented for spicy sauces during food monitoring of 328 mg/kg of total capsaicin (see Table 2) is defined as Scenario 1. In addition, the calculated concentration of Chilli Sauce Sample 3 (2,795 mg/kg of total capsaicin) is used in Scenario 2 and Chilli Sauce Sample 5 with 5,900 mg/kg of total capsaicin in Scenario 3 (see Table 5).

All three scenarios are subdivided into a and b. This is necessary because it cannot be stated with certainty which consumption quantities can be used for the respective sauces. The quantity of 120 g/ portion (equates to 1.89 g/kg of body weight per person) derived from the consumption study and listed in Table 6 is therefore calculated in scenario a. In the b scenarios, on the other hand, it is assumed that the sauces have such a high degree of hotness that they are consumed in smaller quantities than ketchup and other barbecue sauces and that maximum consumption is 2 tablespoons ≈ 30 g of sauce.

The concentrations as well as the quantities consumed per portion are classified as very high. The two figures are multiplied with each other and, in the case of the NVS II data, placed in relation to individual body weight, otherwise to 60 kg per person. This leads to high intake quantity from a single portion.

The intake quantities of capsaicin listed in Table 7 range between 0.2 and 11.2 mg/kg of body weight per portion.

Table 7: High capsaicin intake quantities for the assessment of acute risks in various scenarios

Scenarios			Concentration [mg/kg]	Consumption [g per portion]	Intake [mg per portion]	Consumption [g/kg BW per portion]	Intake [mg/kg BW per portion]
Scenario 1a	Chilli sauce	Highest food monitoring value	328	30	9.8	0.5	0.2
Scenario 1b			328	120	39.4	1.9	0.6
Scenario 2a	Chilli sauce	Chilli Sauce Sample 3	2795	30	83.9	0.5	1.4
Scenario 2b			2795	120	335.4	1.9	5.3
Scenario 3a	Chilli sauce	Chilli Sauce Sample 5	5900	30	177.0	0.5	3.0
Scenario 3b			5900	120	708.0	1.9	11.2

These intake quantities should be compared with scenarios which can be regarded as traditional degrees of hotness. To this end, a high intake through the consumption of fresh chilli fruits is calculated in Scenario 4, taking the maximum capsaicin concentration of 8,550 mg/kg listed in Table 5. Scenario 4a assumes a consumed quantity of chilli fruits equal to the quantity listed in Table 6 of up to 50 g/portion (equivalent to approx. 2 jalapenos). As it is also questionable here, however, whether it is even conceivable to use these quantities for chilli fruits with the highest degree of hotness, it is assumed at the same time that a maximum of 1 small chilli fruit with this degree of hotness is consumed (10 g, because the extremely hot variety of Chilli Sauce Sample 4, for example, weighs considerably less than jalapenos).

Scenario 5 estimates a high intake through chilli as a spice and/or dried chilli fruits and also refers to the maximum value for both groups listed in Table 5 of 3,530 mg/kg and the high consumption quantity of up to 20 g/portion listed in Table 6.

Scenarios 6a and b assume that Tabasco sauce with a concentration of up to 311 mg/kg, which has been an established brand in the market for a long time, is consumed in quantities of ½ to 2 teaspoonsful. The basis for this approach was research conducted in the internet portal www.chefkoch.de. Most of the recipes there use 1 teaspoonful of Tabasco sauce to season dishes for 4 persons, and a few of them use 2 teaspoonsful. This equates to a quantity of one half teaspoonful for Scenario 6a. It was assumed for Scenario 6b that the degree of hotness, which is perceived differently by each individual, can also have the result that some people use more sauce than the recipe recommends, and therefore chose a lump-sum quantity of 2 tablespoonsful per person and portion.

In Scenario 7, the median quantity calculated for the assessment of long-term effects in Mexico of up to 32 mg/d (Lopez-Carrillo 2003) is used as the basis. To extrapolate this value to a quantity per portion, two strong assumptions are made: Firstly, a quantity of one portion per week (Factor 7) is taken and secondly it is assumed that the standard deviation for Mexicans

amounts to the mean value with normal distribution (+ 2 x standard deviation = +2 x 32 = 64 for extrapolation to the upper percentile). The values calculated in this way were then rounded to 300 g/portion and 5 g/kg BW and portion.

Table 8: Capsaicin intake through Tabasco sauce and fresh chilli fruits, derived on the basis of the mean consumption quantities in Mexico, which can still be described as traditional

Scenarios			Concentration [mg/kg]	Consumption [g per portion]	Intake [mg per portion]	Consumption [g/kg BW per portion]	Intake [mg/kg BW per portion]
Scenario 4a	Fresh chilli fruits		8550	50	427.5	0.6	5.1
Scenario 4b	Fresh chilli fruits		8550	10	85.5	0.2	1.4
Scenario 5	Chilli as a spice and/or dried chilli fruits		3530	20	70.6	0.2	0.8
Scenario 6a	Tabasco Sauce	0.5 teaspoon per portion	311	2.5	0.78	0.04	0.01
Scenario 6b	Tabasco Sauce	2 teaspoons per portion	311	10	3.11	0.17	0.05
Scenario 7	High intake in Mexico	Lopez-Carrillo 2003			approx. 300		approx. 5

Scenarios 4 - 7 are presented in Table 8. Comparison of the consumed quantities with those for chilli sauces shows that an intake of up to 5 mg/kg BW per portion can just be interpreted as traditionally handed down degrees of hotness. As hotness is perceived very subjectively and a habituation effect can occur with the frequent consumption of hot and spicy foods, it must be assumed that the maximum tolerable degree of hotness is individually lower for many people.

3.1.3.6 Risk characterization and derivation of recommendations

Experimental findings and human data were compiled on the undesired and toxic effects of acute exposure to hot and very hot *Capsicum* fruits (chilli fruits) and their preparations. These data have to be evaluated under the aspect of which maximum (total) capsaicin concentration appears tolerable in extremely hot and spicy foods sold directly to ultimate consumers and above which it may be necessary to apply a warning notice to the corresponding foods.

3.1.3.6.1 Traditional consumption of hot and very hot chilli fruits and preparations thereof

Concerning the oral intake of chilli fruits and their preparations within the scope of the internationally customary and traditional consumption of dishes flavoured with hot and very hot spices it becomes clear that apart from intolerances due to allergies, no serious health-damaging effects are described in the relevant literature. The known effects associated with the consumption of chillies and their preparations, such as stimulation of salivation, gastric juices, sweat secretion and gastric motility, as well as the perception of heat and burning in the mouth and irritation of the stomach lining, are mentioned in the available literature, how-

ever. It must also be assumed that a habituation effect occurs after repeated chilli consumption, whereby the typical symptoms only appear with higher capsaicin doses, and higher capsaicin concentrations can be tolerated in foods.

Concerning acute exposure, as presented in Table 8, it is assumed that a dose of 5 mg capsaicin/kg BW can still be regarded as the maximum degree of hotness traditionally accepted by adults in a single meal. Scenarios were developed here using the intake of chilli fruits or Tabasco sauce as the basis. In comparisons thereof, intakes of 1.4 - 5.5. mg capsaicin/kg BW were calculated for “extremely hot” chilli sauces with capsaicin concentrations of 2,795 mg/kg or 5,900 mg/kg on the basis of specific consumption quantities, depending on the scenario (Table 7). This explains that on the basis of customary high intake quantities, sauces with up to 6,000 mg of (total) capsaicin/kg (equivalent to 96,000 or roughly 100,000 Scoville units) should equate to the traditional maximum degree of hotness still accepted. The information on the consumption quantities of these “extremely hot” sauces is linked with a high level of uncertainty. The value of 30 g per meal listed in Table 7 as a normally high consumption quantity for these sauces is based on the assumption that these sauces are not consumed in the same quantities as comparable barbecue sauces/ ketchup for which a larger quantity of 120 g per meal was calculated from the consumption data. If the quantity of 120 g per meal were used as the basis, a traditional maximum degree of hotness still accepted for sauces with more than 3,000 mg of (total) capsaicin/kg (equivalent to 48,300 or roughly 50,000 Scoville units) would result.

If the assumed maximum value of 5 mg capsaicin/kg BW for the consumption of a very hot traditional meal is set in relation to data obtained by experimental means, an uncertainty factor of only 1.7 results in relation to the NOAEL (No Observed Adverse Effect Level) of 8.3 mg capsaicin/kg BW with regard to stomach effects in humans (Myers et al., 1987), and a gap of only 12 - 15 to the lowest LD_{50} (oral) of 60 - 75 mg capsaicin/kg BW determined in laboratory experiments on mice.

Based on these observations, the BfR regards a consumption quantity of 5 mg of total capsaicin/kg BW as the maximum dose that should not be exceeded if possible by adults in the course of a meal prepared using chillies or chilli preparations. Express reference is made here to the fact that this maximum dosage can produce undesired effects in individuals who are either sensitive or not used to eating chilli preparations.

3.1.3.6.2 Fiery foods competitions, consumption of extremely hot chillies and their preparations

As reported in the press instances of fiery food eating contests in Germany have resulted in the occurrence of undesired effects, such as extreme nausea and the need for emergency medical treatment like the cases of poisoning in Augsburg in 2010, they were unknown at the responsible institutions contacted. For this reason, an underlying number of unreported/ undetected similar cases must be taken into consideration. Due to this lack of information, the more detailed circumstances of the reported cases of poisoning cannot be analyzed. There is in particular no information on the capsaicin concentration in the product in question, or on the quantities and dilution in which it was ingested and the precise symptoms of poisoning.

The high risk potential of competitions of this kind may possibly be derived from a report in the British media about a death that occurred in a similar situation. Details of the exact circumstances are missing, however, with the result that the causal connection remain unclear and no dose-effect relationships can be derived.

The symptoms of a Texan fiery food eating contest in which the participants had to consume 3-13 jalapeno fruits (median: 5 fruits) within 3 minutes were epiphora, rhinorrhoea, dysuria and a burning sensation during defacation.

More detailed information on the dosage is also lacking in 2 cases in which an arterial hypertensive crisis was diagnosed after the consumption of excessive amounts of “peppers and chili peppers”, one of which occurred with acute myocardial infarction associated with high levels of thyroid stimulating hormone.

Overall, the insufficient data situation does not permit any statements on the dose-effect relationships or on which capsaicin concentrations have to be associated with health-damaging effects in combination with which consumed quantities. Furthermore, reference is made to the fact that it is doubtful whether fiery food eating contests can still be regarded as “normal conditions for the use of a foodstuff” as defined by Article 14 of Reg. (EC) No. 178/2002 or instances of abuse. Irrespective of this, however, in order to reduce the risks involved in contests of this kind, at which extremely hot chilli preparations may be consumed undiluted in exceptionally high quantities, and to lower the risk of accidental poisoning with extremely hot sauces, the limitation of the maximum permissible concentrations of total capsaicin in chilli sauces could be taken into consideration. An orientation aid here could be the above-mentioned maximum limit for total capsaicin intake of 5 mg/kg BW, which can be regarded as the maximum traditionally accepted degree of hotness for one meal. It is therefore questionable whether chilli sauces and chilli extracts with concentrations > 6,000 mg total capsaicin/kg can be regarded in general as safe foods as defined by Art. 14 of Reg. 178/2002 (see 3.1.3.6.1 and Table 7 for the corresponding capsaicin intakes with normally high consumption quantities). Evaluation on a case-by-case basis under consideration of the existing concentration of total capsaicin in combination with the appropriate dilution and dosage recommendations, as well as warning notices, metering devices and child-proof container closures, is regarded as necessary. The fundamental consideration here should be that the normal consumer is generally unaccustomed to handling excessively hot chilli sauces and extracts.

3.1.3.6.3 Exposure of children

From the reports on the lethal poisoning of small children and abusive application with young children, it can be concluded that this age group runs a high risk through exposure to chilli fruits and chilli sauces. The list of symptoms includes shock, acidosis, central cramps, prerenal failure, septicemia, enlargement of the liver, unconsciousness and respiratory restrictions. Here too, the insufficient data situation permits no quantitative risk analysis and for this reason, the appropriate warning notices on the labels, the use of child-proof closures and containers that only dispense small volumes are recommended in principle for chilli sauces which cannot be described as “mild to medium-hot” (concentration: >100 mg total capsaicin/kg).

3.1.3.6.4 Different levels of sensitivity, allergic reactions

Although hypersensitive reactions to cayenne pepper, which can also be triggered by oral exposure, are seldom, they can be life-threatening under certain circumstances. Urticaria, generalized eczema and respiratory complaints have been described as symptoms. With repeated contact with chilli fruits, e.g. in the preparation of food, severe contact dermatitis can occur in the form of burning pains, erythema and hyperesthesia in the palms of the hands (“Hunan hand”). It has to be assumed that persons who seldomly consume chilli fruits and their preparations have a considerably higher sensitivity to capsaicin effects than regular consumers accustomed to capsaicin intake. It is recommended that a note on possible intol-

erance reactions with particularly sensitive consumers should be applied to the labels of hot chilli sauces (concentration: >100 mg total capsaicin/kg).

3.1.3.6.5 Irritation of the skin and mucous membranes

The irritating effect of *Capsicum* fruits and their preparations on the skin and mucous membranes is well documented on the basis of animal experiments and the experiences gained from the pharmaceutical sector regarding the dermal application of formulations containing cayenne pepper preparations. The concentrations of capsaicinoids in liquid preparations amount to 0.005 to 0.01 % and 0.02 to 0.05 % in semi-solid preparations (Commission E, 1990; EP comment, 2011). A burning effect on the intact skin, often combined with heat development and reddening is associated with these concentrations since these local reactions are regarded as part of the therapeutic effect of the medication. A stronger irritating effect can be expected on the mucous membranes than on the skin. For this reason, the BfR recommends that notices should be applied to the packaging of chilli sauces above this concentration range (e.g. > 100 mg total capsaicin/kg). Thus it can be communicated that the product severely irritates the mucous membranes and that in particular, contact with the eyes and damaged skin should be avoided.

3.1.3.6.6 Exposure to pepper spray

Undesired effects (usually affecting the respiratory system) and deaths have been recorded also after the inhalation of pepper spray. While a causal connection with capsaicin exposure is presumed with the death of an asthmatic, a causal relation with other deaths cannot be confirmed. The undesired effects observed after inhalation of capsaicin appear to be relevant to the assessment of capsaicin in foods only to a very limited extent. After inhalation, capsaicin directly enters the bronchial system causing directly undesired effects, such as bronchoconstriction. The LD_{50} determined after the intratracheal administration of capsaicin to mice also showed a significantly lower value than the LD_{50} determined after oral administration (Glinsukon et al., 1980). This suggests that higher doses can be tolerated after oral exposure than after inhalation.

3.2. Scope of action and recommended measures

For the protection of children and sensitive individuals and to prevent skin, mucous membrane and eye irritations, the BfR recommends that label notes and safety closures should be applied to chilli sauces with concentrations > 100 mg total capsaicin/kg.

The BfR also questions whether chilli sauces and chilli extracts with concentrations > 6,000 mg total capsaicin/kg can generally be regarded as safe foods as defined by Art. 14 of Reg. 178/2002 and recommends evaluation on a case-by-case basis (cf. 3.1.3.6.2).

The BfR advises consumers against the intake of unusually large quantities of extremely hot chilli fruits and chilli sauces, such as those encountered in fiery food eating contests, as this can result in health-damaging effects, such as potentially life-threatening hypertensive crises.

Furthermore, the BfR advises that the potentially life-threatening unintentional intake of hot chilli sauces by small children should be avoided.

4. References

Abendzeitung München, 2010. Chili-Noteinsatz: 10 Jugendliche vergiftet, 20.01.2010. http://www.abendzeitung-muenchen.de/inhalt.bayern-chili-noteinsatz:-10-jugendliche-vergiftet.1e564616-6882-49ad-88f4-cbc64acd01c9.html

Albert R, Schneller H (2009). Pflanzenextrakte zur Schädlingsbekämpfung. Landinfo, Vol. 7:1

Bird S (2008). Keen cook died after eating red-hot chilli sauce as a dare. The Times, 29 September. www.timesonline.co.uk/tol/life_and_style/food_and_drink/article

Bozokalfa M K, Esiyok D, Turhan K (2009). Patterns of phenotypic variation in a germplasm collection of pepper (Capsicum annuum L.) from Turkey. Spanish J Agricult Res. 7: 83 - 95.

Bützer P, 2005. Some like it hot. Pädagogische Hochschule St. Gallen http://www.isitech.com/fileadmin/pb/pdf-Dateien/Capsaicin.pdf

Busker RW, van Helden HPM (1998). Toxicologic evaluation of pepper spray as a possible weapon for the Dutch Police Force: risk assessment and efficacy. The American Journal of Forensic Medicine and Pathology, Vol. 19/4: 309-316.

Castle, S, Llanrwst baby saved by first responders after adverse reaction to chilli. North Wales Weekly News; Mar 31,2011. http://www.northwalesweeklynews.co.uk/conwy-county-news/local-conwy-news/2011/03/31/llanrwst-baby-saved-by-first-responders-after-adverse-reaction-to-chilli-55243-28432085/

Choi S-H, Suh B-S, Kozukue E, Kozukue N, Levin C E, Friedman M (2006). Analysis of the Contents of Pungent Compounds in Fresh Korean Red Peppers and in Pepper-Containing Foods. J Agric Food Chem. 54: 9024 - 9031.

Cisneros-Pineda O, Torres-Tapia L W, Gutiérrez-Pacheco L C, Contreras-Martín F, González-Estrada T, Peraza-Sánchez S R (2007). Capsaicinoids quantification in chili peppers cultivated in the state of Yucatan, Mexico. Food Chem. 104: 1755 - 1760.

Committee of Experts on Flavouring Substances, the Council of Europe (Oktober 2005). Active principles (constituents of toxicological concern) contained in natural sources of flavourings.

Dieiil AK, Bauer RL (1978). Jalaproctitis. New England J. Med., Vol. 299/20: 1137-8.

Dikensoy O, Bayram NG, Filiz A (2001). Severe asthma attack in a patient with premenstrual asthma: hot pepper is the possible trigger. Respiration, Vol. 68/2: 227.

Dine MS, McGovern ME (1982). Intentional poisoning of children - an overlooked category of child abuse: report of seven cases and review of the literature. Pediatrics, Vol. 70/1: 32-35.

Environmental Protection Agency - EPA-738-F-92-016 June 1992. EPA R.E.D. Facts, Capsaicin.

Environmental Protection Agency (EPA-HQ-OPP-2010-0796; FRL-8847-6). Capsaicin. Federal Register Vol 75/188, Wednesday, September 29, 2010 Notices: 60116.

Ph. Eur., Europäischen Arzneibuches, 6. Ausgabe (2008); Govi-Verlag, Eschborn.

Ph. Eur.-Commentary , Kommentar zum Europäischen Arzneibuches (2011); Govi-Verlag, Eschborn.

Feldman H, Levy PD (2003). Hot pepper-induced urticaria while repairing a digital laceration. Am. J. Emerg. Med., Vol. 21/2: 159.

Fuller RW, Dixon CM, Barnes PJ (1985). Bronchoconstrictor response to inhaled capsaicin in humans. J Appl Physiol 58:1080-1084.

Gimenez L, Zacharisen M (2011). Severe pepper allergy in a young child. WMJ. Vol. 110/3: 138-9.

Glinsukon T, Stitmunnaithum V, Toskulkao C, Buranawuti T, Tangkrisanavinont V (1980). Acute toxicity of capsaicin in several animal species. Toxicon, Vol. 18: 215-220.

Graham DY, Smith JL, Opekun AR (1988). Spicy food and the stomach. JAMA, Vol. 260/23: 3473.

Hager Rom (2006), Hagers Handbuch der Drogen und arneistoffe, Springer Verlag, Würzburg.

Jesse B (2009). Das Pfefferspray als alltägliches gefährliches Werkzeug. NStZ 2009, 364-beck-online.

Johnson (2007). Final report on the safety assessment of capsicum annuum extract, capsicum annuum fruit extract, capsicum annuum resin, capsicum annuum fruit powder, capsicum frutescens fruit, capsicum frutescens fruit extract, capsicum frutescens resin, and capsaicin. Int. J. Toxicol., Vol. 26 (Suppl .1): 3-106.

Kommission E, Monographie BGA/BfArM (1990). Monographie Capsicum (Paprika). Bundesanzeiger 1.2., Heftnummer 22A, ATC-Code: MO2AB

Kozukue N, Han J-S, Kozukue E, Lee S-J, Kim J-A, Lee K-R, Levein C E, Friedman M (2005). Analysis of Eight Capsaicinoids in Peppers and Pepper-Containing Foods by High-Performance Liquid Chromatography and Liquid Chromatography-Mass Spectrometry. J Agric Food Chem. 53: 9172 - 9181.

Krems C, Bauch A, Götz A, Heuer T, Hild A, Möseneder J, Brombach C (2006). Methoden der Nationalen Verzehrsstudie II. Ernährungs-Umschau. 53: 44 - 50.

Leitner A, Jensen-Jarolim E, Grimm R, Wüthrich B, Ebner H, Scheiner O, Kraft D, Ebner C (1998). Allergens in pepper and paprika. Allergy, Vol. 53: 36-41.

López-Carrillo L, López-Cervantes M, Robles-Díaz G, Ramírez-Espita A, Mohar-Betancourt A, Meneses-García A, López-Vidal Y, Blair A (2003). Capsaicin Consumption, Helicobacter Pylori Positivity and Gastric Cancer in Mexico. Int J Cancer. 106: 277-282.

Martindale: the complete drug reference (2010). Capsaicin. London Pharmaceutical Press.

Max Rubner-Institut (MRI) 2008, Nationale Verzehrsstudie II (NVS II), Ergebnisbericht 1, 2 http://www.was-esse-ich.de/

Milke P, Diaz A, Valdovinos MA, Moran S (2006). Gastroesophageal reflux in healthy subjects induced by two different species of chilli (Capsicum annum). Dig. Dis., Vol. 24: 184-188.

Myers BM, Smith JL, Graham DY (1987). Effect of red pepper and black pepper on the stomach. Am. J. Gastroenterol., Vol. 82/3: 211-4.

New Scientist (2008). How chilis can kill.
http://www.newscientist.com/blogs/shortsharpscience/2008/09/how.

Nopanitaya W, Nye SW (1974). Duodenal mucosal response to the pungent principle of hot pepper (Capsaicin) in the rat: light and electron microscopic study. Toxicology and Appl. Pharmacology, Vol. 30: 149-161.

NPIC (National Pesticide Information Center) 1.800.858.7378 - NPIC (2011). Capsaicin Technical Fact Sheet

Olajos EJ, Salem H (2001). Riot control agents: pharmacology, toxicology, biochemistry and chemistry. J. Appl. Toxicology, Vol. 21: 355-391.

Patanè S, Marte F, La Rosa FC, La Rocca R (2010). Capsaicin and arterial hypertensive crisis. Int. J. Cardiology, Vol. 144: e26-e27.

Patanè S, Marte F, Di Bella G, Cerrito M, Coglitore S (2008). Capsaicin, arterial hypertensive crisis and acute myocardial infarction associated with high levels of thyroid stimulating hormone. Int. J. Cardiology, Vol. 134/1: 130-2.

Pena-Alvarez A, Ramirez-Maya E, Alvarado-Suárez L (2009). Analysis of capsaicin and dihydrocapsaicin in peppers and pepper sauces by solid phase microextraction gas chromatography mass spectrometry. J Chromatogr A. 1216: 2843 - 2847.

Perucka I, Oleszek W (2000). Extraction and determination of capsaicinoids in fruit of hot pepper Capsicum annuum L. by spectrophotometry and high-performance liquid chromatography. Food Chem. 71: 287 - 291.

Peter KV (2001). Handbook of herbs and spices. Volume 1, Woodhead Publishing Series in Food Science, Technology and Nutrition: Number 63. Woodhead Publishing Limited, Oxford, Cambridge, New Delhi, CRC Press Boca Raton, Boston, New York, Washington, DC.

M. Peusch, E. Muller-Seitz, M. Petz, A. Muller and E. Anklam, Extraction of capsaicinoids from chilies (Capsicum frutescens L.) and paprika (Capsicum annuum L.) using spercritical fluids and organic solvents. Zeitschrift fur Lebensmittel-Untersuchung und-Forschung A, 204 (1997), pp. 351-355.

Rance F, Dutau G (1997). Labial food challenge in children with food allergy. Pediatr. Allergy Immunol., Vol. 8: 41-44.

Rettungsdienst.de, 2010. Vergiftung durch Chili-Sauce
http://www.rettungsdienst.de/nachrichten/vergiftung-durch-chili-sauce-14510

Roth K (2010). Die Skala des Wilbur Lincoln Scoville. Chem. Unserer Zeit, Vol. 44: 138-151.

Rugwani RM, Blomquist PH (2002). Ultraviolet dye masquerading as corneal abrasion. American Journal of Emergency Medicine, Vol. 20/4: 383-4.

Saito A, Yamamoto M (1996). Acute oral toxicity of capsaicin in mice and rats. J. Toxicol. Sci., Vol. 21: 195-200.

Salter J (2008). Chef dies after eating “superhot” chilli for bet. The Telegraph, 29. Sept.
www.telegraph.co.uk/news/uknews/3099484/Chef-dies-after-eating...

SCF (2002) Opinion of the Scientific Committee on Food on Capsaicin (adopted on 26 February 2002)
http://europa.eu.int/comm/food/fs/sc/scf/out120_en.pdf

Schöll I, Jensen-Jarolim E (2004). Allergenic potency of spices: hot, medium hot, or very hot. Int. Arch. Allergy Immunol., Vol. 135/3: 247-61.

ShortNews, 2010. Gefährliche Mutprobe: Vergiftungen durch Chili-Sauce, 20.01.10.
http://www.shortnews.de/id/810537/Gefaehrliche-Mutprobe-Vergiftungen-durch-Chili-Sauce

Smith J, Greaves I (2002). The use of chemical incapacitant sprays: a review. J. Trauma., Vol. 52: 595-600.

Smith CG, Stopford W (1999). Health hazards of pepper spray. NCMJ, Vol. 60/5: 268.

Snyman T, Stewart MJ, Steenkamp V (2001). A fatal case of pepper poisoning. Forensic Science International, Vol. 124: 43-46.

Steffee CH, Lantz PE, Flannagan LM, Thompson RL, Jason DR (1995). Oleoresin capsicum (pepper) spray and “in-custody deaths”. Am. J. Forensic Med. Pathol., Vol. 16/3: 185-192.

Takahashi K, Nishime A, Kakinuma M, Koitabashi Y, Sugaya A, Tanifuji F, Miyamoto T (2008). Pungent and aroma substances of koreigusu sauce from Okinawa [Japan] (Abstract, Aufsatz in Japanisch). J Japan Soc Food Sci Technicol

Ternes W, Täufel A, Tunger L, Zobel M (2007). Lexikon der Lebensmittel und der Lebensmittelchemie. Wissenschaftliche Verlagsgesellschaft mbH Stuttgart.

Teuscher E, Triebes M, Melzig F, Lindequist U (2004). Biogene Arzneimittel. 6. Auflage, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart.

Thapa B, Skalko-Basnet N, Takano A, Masuda K, Basnet P (2009). High-Performance Liquid Chromatography Analysis of Capsaicin Content in 16 Capsicum Fruits from Nepal. J Med Food. 12: 908 - 913.

Thomas B V, Schreiber A A, Weisskopf C P (1998). Simple Method for Quantitation of Capsaicinoids in Peppers Using Capillary Gas Chromatography. J Agric Food Chem. 46: 2655 - 2663.

Tominack RL, Spyker DA (1987). Capsicum and capsaicin - a review: case report of the use of hot peppers in child abuse. Clinical Toxicology, Vol. 25/7: 591-601.

TZ-Online, 2010. Mutprobe mit Höllen-Sauce: Acht Schüler in der Klinik 20.01.10. http://www.tz-online.de/nachrichten/bayern/grosseinsatz-rettungsdienst-augsburg-jugendliche-chili-sauce-vergiftet-meta-598249.html

US EPA: National Center for Environmental Assessment, Office of Research and Development: Exposure Factors Handbook..Expsosure Assessment Division, Versar Inc., Springfield, VA, USA 1997

Vesaluoma M, Müller L, Gallar J, Lambiase A, Moilanen J, Hack T, Belmonte C, Tervo T (2000). Effects of oleoresin capsicum pepper spray on human corneal morphology and sensitivity. Investigative Ophthalmology & Visual Science, Vol. 41/8: 2138-2147.

Watson WA, Stremel KR, Westdorp EJ (1996). Oleoresin capsicum (cap-stun) toxicity from aerosol exposure. The Annals of Pharmacotherapy, Vol. 30: 733-735.

Williams SR, Clark RF, Dunford JV (1995). Contact dermatitis associated with capsaicin: hunan hand syndrome. Ann. Emerg. Med., Vol. 25/5: 713-5.

Winek CL, Markie DC, Shanor SP (1982). Pepper sauce toxicity. Drug and Chemical Toxicology, Vol. 5/2: 89-113.

Yeoh KG, Ho KY, Guan R, Kang JY (1995). How does chilli cause upper gastrointestinal symptoms? J. Clin. Gastroenterol., Vol. 21/2: 87-90.

Zoschke H, 2011. Peperworld http://www.pepperworld.com/

Zuskin E, Schachter EN, Kanceljak B, Mustajbegovic J, Witek TJ (1994). Immunological and respiratory reactions in workers exposed to organic dusts. Int. Arch. Occup, Environ. Health, Vol. 66: 317-324.